

Applicant : Shawn Shui-On Leung  
U.S. Serial No.: 09/892,613  
Filed : June 27, 2001  
Page : 2

In the claims:

Claims 1-39 and 50 (Cancelled)

40. (Currently Amended) A re-engineered, or framework (FR)-patched immunoglobulin containing a heavy or light or heavy and light chain variable regions sequences from a parent antibody, in which at least one of the compartmentalized framework sequences, defined as FR1, FR2, FR3 and FR4 are replaced, or patched by the corresponding compartmentalized framework sequences from the heavy or light or heavy and light chain immunoglobulin variable region of a different species, respectively, wherein said re-engineered immunoglobulin comprises compartmentalized framework sequences—derived from at least two different sources of different immunoglobulin chains, wherein said different immunoglobulin chains can be sourced from different immunoglobulins of the same species, or from different immunoglobulins of different species, and such re-engineered immunoglobulin binds specifically to an antigen with affinity within 3-fold of that of the parent immunoglobulin with the proviso that not all the replaced FR1, FR2 and FR3 of the re-engineered immunoglobulin heavy chain are from the same framework of a single immunoglobulin heavy chain;—whereas and not all the replaced FR1, FR2 and FR3 of the re-engineered immunoglobulin light chain are from the same framework of a single immunoglobulin light chain.

41. (Original) A re-engineered or FR-patched immunoglobulin according to Claim 40, in which the particular FR chosen for

Applicant : Shawn Shui-On Leung  
U.S. Serial No.: 09/892,613  
Filed : June 27, 2001  
Page : 3

patching or replacing each corresponding FR in the parent immunoglobulin:

- a. exhibits the highest degree of homology, or at least 60%, to the corresponding parent FR;
- b. exhibits identical sequence homology to the corresponding parent FR at the three amino acids immediately adjacent to the flanking CDR's; and
- c. contains identical amino acid to the corresponding parent FR at positions known to be close to, or have interactions with the CDR's/antigen binding site, as evaluated by computer modeling, crystal structure, published information, or prior experience.

42. (New) A re-engineered, or FR-patched immunoglobulin according to Claim 40, in which the particular FR chosen for patching or replacing each corresponding FR in the parent immunoglobulin:

- a. exhibits the highest degree of homology, or at least 60%, to the corresponding parent FR;
- b. exhibits identical sequence homology to the corresponding parent FR at the four amino acids immediately adjacent to the flanking CDR's; and
- c. contains identical amino acid to the corresponding parent FR at positions known to be close to, or have interactions with the CDR's/antigen binding site, as

Applicant : Shawn Shui-On Leung  
U.S. Serial No.: 09/892,613  
Filed : June 27, 2001  
Page : 4

evaluated by computer modeling, crystal structure, published information, or prior experience.

43. (Original) A re-engineered or FR-patched immunoglobulin according to Claim 40, in which the particular FR chosen for patching or replacing each corresponding FR in the parent immunoglobulin:

- a. exhibits the highest degree of homology, or at least 60%, to the corresponding parent FR;
- b. exhibits the highest degree of sequence homology to the corresponding parent FR, preferably identical, or contains conservatively similar amino acids at the three amino acids immediately adjacent to the flanking CDR's; and
- c. contains identical, or conservatively similar amino acids to the corresponding parent FR at positions known to be close to, or have interactions with the CDR's/antigen binding site, as evaluated by computer modeling, crystal structure, published information, or prior experience.

44. (Original) A re-engineered or FR-patched immunoglobulin according to Claim 40, in which the particular FR chosen for patching each corresponding FR in the parent immunoglobulin:

- a. exhibits the highest degree of homology, or at least 60%, to the corresponding parent FR;

Applicant : Shawn Shui-On Leung  
U.S. Serial No.: 09/892,613  
Filed : June 27, 2001  
Page : 5

- b. exhibits the highest degree of sequence homology to the corresponding parent FR, preferably identical, or contains conservatively similar amino acids at the four amino acids immediately adjacent to the flanking CDR's; and
- c. contains identical, or conservatively similar amino acids to the corresponding parent FR at positions known to be close to, or have interactions with the CDR's/antigen binding site, as evaluated by computer modeling, crystal structure, published information, or prior experience.

45. (Original) A re-engineered, or FR-patched immunoglobulin according to Claim 40, containing the heavy or light or heavy and light chain variable region sequences from a parent antibody, in which the particular FR chosen for patching each corresponding FR in the parent immunoglobulin comprises amino acids derived from the parent immunoglobulin framework outside the Kabat and Chothia CDRs, wherein the parent amino acids replace corresponding amino acids in the patching FR, wherein the patching FR is the FR derived from a different source used for patching, or that replaces the original FR of, the parent immunoglobulin.

46. (Original) A re-engineered, or FR-patched immunoglobulin according to Claim 40, which specifically binds to an antigen with an affinity of between  $10^7 M^{-1}$  and  $10^{11} M^{-1}$ .

Applicant : Shawn Shui-On Leung  
U.S. Serial No.: 09/892,613  
Filed : June 27, 2001  
Page : 6

47. (Original) A re-engineered, or FR-patched immunoglobulin according to Claim 40, which specifically binds to an antigen with an affinity of between  $10^8 \text{ M}^{-1}$  and  $10^{10} \text{ M}^{-1}$ .

48. (Currently Amended) A re-engineered or FR-patched immunoglobulin according to Claims 40, which is substantially pure.

49. (Original) A pharmaceutical composition comprising a re-engineered or FR-patched immunoglobulin according to Claim 40, in a pharmaceutically acceptable carrier.

50. (Cancelled)